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Item 1 of the Office Action - Claim Objections

The Examiner has objected to claims 25 and 26 because of the use of parentheses Applicant has amended claims 25 and 26 by deleting the within the claims.

parentheses. Applicant respectfully submits that the objections have been overcome.

Item 2 of the Office Action - Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 5 under 35 U.S.C. § 112, second paragraph as

allegedly indefinite for failing to particularly point out and distinctly claim the subject

matter which Applicant regards as the invention. In particular, the Examiner believes

that the expression "a method of preventing myocardial infarction" renders the claim

indefinite. In addition, the Examiner has indicated that he would favorably consider the

term "prophylaxis" over "prevention".

Although Applicant respectfully disagrees, to move the prosecution of this case forward,

Applicant has amended claim 5 to indicate that the RAR antagonist or RAR inverse

Accordingly, Applicant agonist act as a prophylaxis for myocardial infarction.

respectfully submits that the rejection of claim 5 has been overcome.

Item 3 of the Office Action - Rejection Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-6, 11, 12, 16, and 22-26 under 35 U.S.C. § 103(a)

as allegedly being unpatentable over Klein (U.S. Pat. No. 5,776,699) in view of Aberg

(Atherosclerosis, 1985). In particular, the Examiner contends that Klein teaches a

group of RAR antagonists, including the elected compound AGN 194310, as being

useful in inhibiting hypertriglycerides. The Examiner acknowledges that Klein fails to

specifically teach the employment of AGN 194310 in a method of lowering triglyceride.

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or specifically teach a method of preventing myocardial infarction. The Examiner states that Aberg teaches that elevated serum triglyceride is one of the risk factors of developing myocardial infarction.

The Examiner believes that one skilled in the art would have been motivated to employ AGN 194310 in a method of lowering triglyceride level and preventing myocardial infarction because RAR antagonists of Klein are known to be useful in inhibiting hypertriglyceridemia, and that, employing any RAR antagonists of Klein, including AGN 194310, would have been reasonably expected to be useful in a method of lowering triglyceride level. The Examiner further believes that because it is allegedly known that elevated serum triglyceride levels increase the risk of developing myocardial infarction, patients taking AGN 194310 to lower their serum triglyceride level would be reasonably expected to prevent the development of myocardial infarction.

Applicant has considered the Examiner's position and respectfully traverses the rejections.

Klein states that the compounds disclosed therein "can block hypertriglyceridemia caused by coadministered retinoids" (column 20, line 65 to column 21, line 1). In addition, Klein provides one example of a RAR antagonist, AGN 193109, that does not appear to decrease naturally occurring serum triglyceride levels (see Example 4, Table 10, group B). The RAR antagonists of Klein are disclosed as capable of preventing increases of serum triglyceride levels. For example, the RAR antagonists of Klein are disclosed as potential antidotes for retinoid compounds in conditions such as hypervitaminosis A and retinoid toxicity. In other words, the RAR antagonists of Klein may generally be used to block increases of triglyceride levels caused by retinoids. Klein does not specifically disclos, teach, or suggest the present invention. example. Klein does not specifically disclose or even suggest RAR antagonists to treat hyperlipidemia. Klein states that "sufficient quantities of the RAR antagonist be present Applicant: Yuan et al. Serial No.: 09/848,159

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continuously in the tissue of interest during exposure to the RAR agonist<sup>-</sup> (column 6, lines 18-21). One interpretation of the disclosure of Klein is that preventing an increase in triglyceride levels caused by retinoids by using a RAR antagonist may be attributed to blocking the actions of the retinoid on the retinoid receptors. In any event, Klein does not specifically disclose or even suggest the use of RAR antagonists for treating hyperlipidemia, as recited in the present claims.

Because Klein does not specifically teach or suggest the present invention of treating hyperlipidemia, one skilled in the art would not be motivated by Klein alone to use RAR antagonists, including AGN 194310, to treat hyperlipidemia, let alone be motivated to combine the teachings of Klein with those of Aberg to prevent myocardial infarction. If anything, one skilled in the art would actually be motivated to try different compounds instead of RAR antagonists. As indicated above, given the teachings of Klein, one skilled in the art may actually expect that Klein's RAR antagonists may be sufficient to prevent increases in triglyceride levels.

In view of the foregoing, Applicant respectfully submits that claims 1-6, 11, 12, and 22-26 are unobvious and patentable over Klein in view of Aberg under 35 U.S.C. § 103(a). Thus, Applicant respectfully submits that the claims are in condition for allowance, and respectfully requests that the above-identified application be passed to issuance at an early date.

In addition, Applicant maintains the right to pursue the subject matter of the non-elected species in the above-identified application upon an indication that a generic claim, such as claim 1, is determined to be allowable.

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If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned representative invites the Examiner to telephone either Greg S. Hollrigel, Ph.D. or Quan Nguyen at the number provided below.

Respectfully submitted,

Date: 12/27/01

Frank J. Uxe

Attorney for Applicant Registration No. 25,612 4 Venture, Suite 300 Irvine, California 92618

(949) 450-1750

(949) 450-1764 Facsimile

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being transmitted via facsimile to the Commissioner for Patents in Washington. DC 20231, to fax number 703-308-4556, on or before. December 27, 2001

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

## In the Claims:

Claims 5, 25, and 26 have been amended as follows:

- 5. (Amended) A method of claim 1 wherein said RAR antagonist or an RAR inverse agonist acts as a prophylaxis of myocardial infarction.
- 25. (Amended) A method for treating hyperlipidemia in a mammal, said method comprises a step of administering to said mammal an effective amount of 4-[[4-(4-ethylphenyl)-2.2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid.
- 26. (Amended) A method of claim 24 wherein the step of administering 4-[[4-(4-ethylphenyl)-2.2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid lowers the level of circulating triglycerides.